

JUL 20 1999

**FREEDOM OF INFORMATION SUMMARY
FOR
COMPONENT® E-H (Progesterone and Estradiol Benzoate)**

1. GENERAL INFORMATION

NADA Number: 135-906

Sponsor: Ivy Laboratories
Division of Ivy Animal Health, Inc.
8857 Bond Street
Overland Park, KS 66214

Generic Name: Testosterone Propionate, Estradiol Benzoate, and Tylosin Tartrate

Trade Name: Component® E-H with Tylan®

Marketing Status: Over-the-counter (OTC)

Effect of Supplement: This supplement provides for the addition of a tylosin tartrate pellet as a local antibacterial to Component® E-H.

2. INDICATIONS FOR USE

For growth promotion and improved feed efficiency in heifers weighing 400 lbs or more.

3. DOSAGE FORM(S), ROUTE OF ADMINISTRATION, AND RECOMMENDED DOSAGE

Dosage Form: Implantation

Route of Administration: Subcutaneous implantation on the posterior aspect of the middle one-third of the ear by means of an implant gun.

Recommended Dosage: One implant containing 200 mg testosterone propionate, 20 mg estradiol benzoate, and 29 mg tylosin tartrate.

4. EFFECTIVENESS

The effectiveness requirement for this supplemental new animal drug application, with the indications for use and dosage as given in Sections 2 and 3 above, is met by utilizing the existing database in NADA 135-906 and conducting the additional adequate and well-controlled study included in this supplemental application.

Pivotal Study:

A study was conducted by William Barton, CAVL, Inc, Amarillo, TX, to evaluate the effectiveness of Component[®] E-H with Tylan[®] to lower the incidence of ear abscess formation. An implant site abscess induction model was developed to reliably create a high abscess rate in test animals. This model was used to test the ability of a tylosin tartrate pellet to reduce implant site abscess incidence in animals expected to develop an ear abscess. In the study, 40 beef heifers were subjected to the abscess-inducing culture at the same time they were implanted with either Component[®] E-H with a Tylan[®] pellet or Component[®] E-H alone. Implant sites were observed at regular intervals up to 35 days following implantation. Abscess rate at each time point was significantly lower ($P < 0.0001$) in heifers treated with Component[®] E-H with a Tylan[®] pellet compared to heifers treated with Component[®] E-H alone, with the maximum incidence of abscesses of 0% and 90%, respectively.

5. TARGET ANIMAL SAFETY

Target animal safety of Component[®] E-H is established by data in the parent application. The data provided in the effectiveness study described above was sufficient to conclude that the use of the tylosin pellet was safe for use in cattle. No further studies were required.

6. HUMAN SAFETY

Human safety is established for Component[®] E-H by data in the parent application. No further studies were required for use of the tylosin pellet.

7. AGENCY CONCLUSIONS

Adequate data demonstrates the safe and effective use of a tylosin tartrate pellet added to Component[®] E-H as a local antibacterial.

Under the Center's supplemental approval policy (21 CFR 514.106(b)(2)), this is a Category II change providing for the addition of a tylosin tartrate pellet as a local antibacterial to Component[®] E-H. The approval of this change is not expected to have any adverse effect on the safety or effectiveness of this new animal drug. Accordingly, this approval did not require a reevaluation of the safety and effectiveness data in the parent application.

8. LABELING

Facsimile labeling is attached as follows:

1. Component[®] E-H with Tylan[®] Box Label
2. Component[®] E-H with Tylan[®] 20 Dose Foil Pouch
3. Component[®] E-H with Tylan[®] Package Insert



Fold & Seal Area Print Optional

Front Panel

Bleed 1 color only

COMPONENT[®] E-H
BRAND IMPLANTS HEIFER IMPLANTS
testosterone propionate USP 200 mg and estradiol benzoate 20 mg
with 29 mg tylosin tartrate as a local antibacterial



TEAR HERE

COMPONENT[®] E-H Implants are recommended for use in heifers weighing 400 lbs. or more for growth promotion and improved feed efficiency.

Contains: One Cartridge Belt of 20 implants each sealed in a sanitary foil pouch. Each dose consists of testosterone propionate USP 200 mg and estradiol benzoate 20 mg with 29 mg tylosin tartrate as a local antibacterial.

* Patented by Ivy Laboratories, Inc. NADA 135-906, Approved by FDA

Bleed 1 color only

Bleed 1 color only

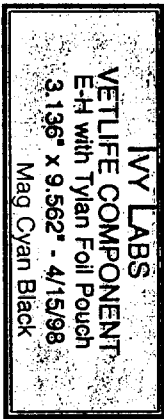
One 20-Dose Cartridge Belt



Bleed 1 color only



Fold & Seal Area Print Optional





Fold & Seal Area Print Optional

Back Panel



Bleed 1 color only

Bleed 1 color only

WARNING: Implant one dose - 8 pellets (entire contents of one cartridge) - in the ear subcutaneously. Any other site of implantation is in violation of Federal Law. DO NOT attempt to salvage implantation site for animal feed or human food.

CAUTION: For Heifer use only. Bulging, vaginal and rectal prolapse, udder development, ventral edema and elevated tail-heads have occasionally been reported in heifers implanted with testosterone propionate and estradiol benzoate.
Important: Read the enclosed instruction brochure. Use as illustrated with a CAREFUL CLEAN TECHNIQUE. Never take short cuts at the expense of CLEANLINESS.

RESTRICTED DRUG - USE ONLY AS DIRECTED (CALIFORNIA) - FOR USE IN ANIMALS ONLY
NOT FOR HUMAN USE - KEEP OUT OF REACH OF CHILDREN

Store at controlled room temperature - 15°-30°C (59°-86°F).
DO NOT refrigerate - avoid excessive heat and humidity.

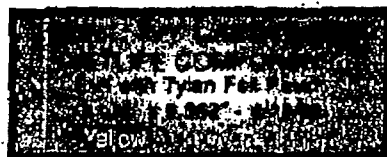
Manufactured by a non-sterilizing process.

COMPONENT is a registered trademark of Ivy Laboratories, Inc.
Tylan is a registered trademark of Eli Lilly and Company
Manufactured for: VetLife L.L.C., Overland Park, KS 66214, USA by Ivy Laboratories, Inc.
01 22 02 00

PURCHASE SEAL
20 IMPLANTS

Bleed 1 color only

Bleed 1 color only



20 DOSES FOIL POUCH
BACK

TEAR HERE

**RESTRICTED DRUG - USE ONLY AS DIRECTED (CALIFORNIA) - FOR USE IN ANIMALS ONLY
NOT FOR HUMAN USE - KEEP OUT OF REACH OF CHILDREN**

Important: Read enclosed instruction brochure and follow directions.

Store at controlled room temperature - 15°-30°C (59°-86°F). DO NOT refrigerate - avoid excessive heat and humidity.

COMPONENT® E-H

BRAND IMPLANTS HEIFER IMPLANTS

testosterone propionate USP 200 mg and estradiol benzoate 20 mg
with 29 mg tylosin tartrate as a local antibacterial



COMPONENT® E-H Implants are recommended for use in heifers weighing 400 lbs. or more for growth promotion and improved feed efficiency.

Contains: 5 Cartridge Belts* of 20 implants each. Each dose consists of testosterone propionate USP 200 mg and estradiol benzoate 20 mg with 29 mg tylosin tartrate as a local antibacterial.

* Patented by Ivy Laboratories, Inc. NADA 135-906, Approved by FDA

100 IMPLANTS



WARNING: Not for use in dairy or beef replacement heifers. Implant one dose - 9 pellets (entire contents of one cartridge) - in the ear subcutaneously. Any other site of implantation is in violation of Federal Law.
DO NOT attempt to salvage implantation site for animal feed or human food.

Caution: For use in Heifers only. Bulling, vaginal and rectal prolapse, udder development, ventral edema and elevated tail-heads have occasionally been reported in heifers implanted with testosterone propionate and estradiol benzoate.

Important: Read the enclosed instruction brochure. Use as illustrated with a CAREFUL CLEAN TECHNIQUE. Never take short cuts at the expense of CLEANLINESS.

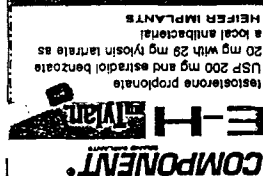
Manufactured by a non-sterilizing process.

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Manufactured for: **VetLife L.L.C.**, Overland Park, KS 66214, USA by Ivy Laboratories, Inc.

01 22 03 00



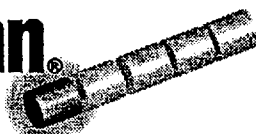
100 DOSES CARTON
REDUCED TO 75%

COMPONENT®
ISLAND IMPLANTS

VetLife

E-H WITH Tylan®

HEIFER IMPLANTS



testosterone propionate USP 200 mg and
estradiol benzoate 20 mg with 29 mg tylosin
tartrate as a local antibacterial

20 dose CARTRIDGE BELT*

For use with the COMPONENT® One Gun™**
For Use in Animals Only

Each CARTRIDGE BELT holds 20 doses of COMPONENT® E-H Implants. Each dose of 9 pellets consists of 8 pellets containing a total of 200 mg testosterone propionate USP and 20 mg estradiol benzoate plus 1 pellet containing 29 mg tylosin tartrate as a local antibacterial. COMPONENT® E-H Implants are recommended for use in heifers weighing 400 lbs or more for INCREASED RATE OF WEIGHT GAIN AND FEED EFFICIENCY.

Manufactured by a non-sterilizing process.

GENERAL INSTRUCTIONS:

Study the instructions which should be followed carefully at all times, avoiding short cuts. Skin infection can be avoided by properly preparing implant site and implanter. During fly season use fly repellent on implant site. One designated team member should always do the implanting. Cleanliness of hands and instruments is important at all times.

WARNING

Not for use in dairy or beef replacement heifers. Implant pellets in ear only. Any other site is in violation of Federal Law. Do not attempt to salvage implant site for animal feed or human use.

KEEP THIS AND ALL OTHER DRUGS
OUT OF REACH OF CHILDREN.

Restricted Drug—Use Only As Directed (California)

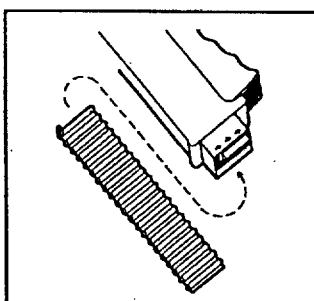
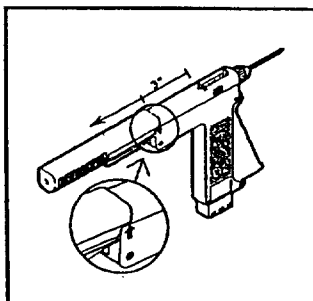
CAUTION:

For use in heifers only. Bulling, vaginal and rectal prolapse, udder development, ventral edema and elevated tail-heads have occasionally been reported in animals implanted with testosterone propionate and estradiol benzoate.

IMPLANTING INSTRUCTIONS:

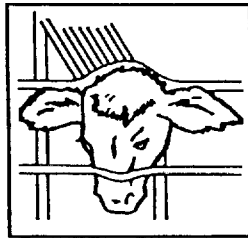
Loading the Implanter

Load the implanter following the instructions supplied with each implanter.



Restrain the Animal

Speed of implantation as well as safety of handlers is best achieved by restraining animal in a squeeze chute using head restraint. When implanting horned cattle, better control is obtained with additional use of nose tongs.

**Prepare the Implant Site**

Scrub the back side of the ear (implant site) with a piece of clean absorbent cotton which has been soaked with a germicidal solution. Follow manufacturer's directions on germicide for correct strength and preparation of solution. Avoid getting into animal's eyes.

Where to Implant

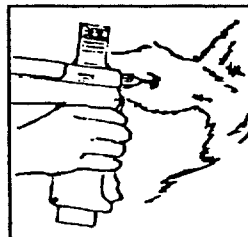
The full contents of the cartridge should be implanted beneath the skin on the back side of the middle one-third of the ear as illustrated in the drawing. The implant must not be closer to the head than the edge of the auricular cartilage ring farthest from the head. The location for insertion of the needle is a point toward the tip of the ear and at least a needle length away from the intended deposition site.



Avoid injuring the large arteries, veins and cartilage of the ear.

Insert the Needle

With one hand firmly grasp the ear. With other hand insert needle point through the skin and ease forward on a lateral plane until the entire length of the needle is under the skin.

**Implant the Pellets**

After inserting the needle fully in the correct implant position squeeze the trigger fully. As the needle is withdrawn from the ear, the controlled-pressure plunger action properly deposits the implant in the needle track. This procedure should prevent breakage or crushing of pellets if otherwise forced into contact with tough fibrous-tissue underlying the skin. The length and total contact area of a single dose are designed to permit absorption of the hormones after implantation to stimulate good weight gain. Broken or crushed pellets may interfere with rates of gain and may lead to undesirable side effects such as noted in the CAUTION.

Clean the Needle

Clean the implanter needle with alcohol or a properly diluted germicidal solution prior to implanting the next animal.

Store at controlled room temperature 15° to 30°C (59° to 86° F)

DO NOT refrigerate – avoid excessive heat and humidity.

NADA 135-906, Approved by FDA

*U.S. Patent No. 4,531,938

**U.S. Patent Nos. 4,762,515 & 5,522,797 – Ivy Animal Health, Inc.

COMPONENT E-H with Tylan is covered by U.S. Patent No. 5,874,098

COMPONENT is a registered trademark of Ivy Animal Health, Inc.

Tylan is a registered trademark of Eli Lilly and Company.

Manufactured for VetLife by Ivy Laboratories.

Overland Park, KS 66214, USA

VetLife and Ivy Laboratories are divisions of Ivy Animal Health, Inc.